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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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ROSS J. OEHLER
AVENTIS PHARMACEUTICALS INC.
ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
PATEL, SUDHAKER B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,092	BOUCHARD ET AL.	
	Examiner	Art Unit	
	Sudhaker B. Patel, D.Sc.Tech.	1624	

-- Th MAILING DATE of this communication appears on the cover sheet with th correspondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application has been transferred to undersigned examiner in Art Unit 1624 from the earlier art unit 1617.

Election/Restrictions

Restriction withdrawn:

Applicant's election with traverse of invention of Group I in Paper No. 7 dated 3/4/03,is acknowledged. Applicants' arguments and remarks have been considered, and found persuasive. Therefore, the restriction/election is now withdrawn. The claims in this application are the claims 1-10, which are related to compounds, 11-12, which are related to process of making the compounds, 13, which is related to composition, 14 which is related to method of use. Therefore, the claims under consideration are the claims 1-14.

After further review and reconsideration, this application is found not ready for the allowance at this stage for the reasons stated bellow.

First action on merits follows.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A). Claims 1-9 recite as:" A product of general Formula or Formulae (where applicable) or a product according to the preceding claim". Correction to:" A compound of " and " claim 2 or claim 3" is required.

(B). Claims 1-10, 11,13,14 recite:" A product" and "or salt thereof". Correction to "A compound" and " pharmaceutically acceptable salt" thereof is required.

(C). Claims 1 recites:" Alkyl and cycloalkyl". The claim does not exactly say about the nature, size, and degree of saturation of the groups. Specification on page4 in lines 1-10 defines these terms. Are branched alkyls and saturated 5- membered cycloalkyls are excluded? Corrections to: " Alkyl consisting of 1 to 6 carbon atoms and cycloalkyl consisting of 5 or m6 membered saturated cycloalkyl rings" is required.

(D). Claim 10 recites:" chemical formula of a compound". Correction to:" A compound of claim 1" is required.

(E). Claims 13 recites:" A medicament comprising as active principal a product according to claim 1 and an excipient". Correction to:" A pharmaceutical composition.... A compound according to claim 1 and an pharmaceutically acceptable excipient" is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claim14 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a step/process asserted utility or a well-established utility.

The claim remains silent about the exact process/step of administration, exact dosage regimen, and the who is at the receiving end for such prevention or treatment.

Claim 14 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a step/process asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

See rejection bellow.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating diabetes, does not reasonably provide enablement for preventing diabetes and a complication of diabetes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

7. The specification in pages 17-19 recite various forms of diabetes and various complications in different forms, and the claims as recited does not represent a single, exact and definite disease. e.g. Type II diabetes or cardiomyopathy. The claim includes diseases and complication related to various body organs. e.g. left ventrical, lower limbs, sexual impotence, diabetic neuropathy in its various forms, pain, ulcers of the foot, elimination of cholestrol from the atheroma, inhibition of oxidation of the LDLs,

normalization of the fatty acids, obesity and the complications and diseases yet to be discovered.

8. In cases directed to chemical compounds, which are being used for their physiological/biological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See in re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group and In re Wiggins 179 USPQ 421.

9. "Stereoisomeric form(s) or Salt(s) with an inorganic or organic acid" as recited in the claims read on all such moieties regardless of complexity of structure and point of attachment to the aliphatic or carbocyclic or non-aromatic core or bridge/chain for which there is no sufficient teaching how to make and how to use at any one selective location among the many possible sites present. The situation is more confusing when a skilled person in the art tries to visualize the multiple possibilities of combining a compound of claim 1(or claims dependent on it) and/ or its composition in its "Stereoisomeric form(s) or Salt(s) with an inorganic or organic acid". Applicants provide no reasonable assurance that any and all derivatives of the instant compounds and their combinations either alone or in a combination therapy as outlined in specification page 19, lines 9-16, will have ability to generate the compounds in vivo or in vitro by one or more processes.

10. In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ 2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include:***(1).*** The nature of invention;***(2).*** the state of prior art ;***(3).*** the predictability

or lack thereof in the art; ***(4).*** the amount of direction or guidance present; ***(5).*** the presence or absence of working examples; ***(6).*** the breadth of the claims, and ***(7).*** the quantity of experimentation needed.

11. Following references are cited to show the state of art for a few diseases/complications.

- Clinical efficacy of Art recognized compound, sildenafil citrate, and predictors of long-term response:

Gonzalgo et at(PubMed Abstract 12853809, also cited as J. Urol., 170/2, 503-6(2003)) state that:"SC remains a highly effective and durable agent for ED.... Patients who discontinued SC reported significantly decreased sexual function than their counterparts but under used alternative therapies to improve ED".

- Erectile physiological and pathophysiological pathways involved in ED:

Andersson Ke(PuBmed Abstract 12853766, also cited as J. Urol. 170/2,6-14(2003)) state that:" Diffetent types of ED often have overlapping pathophysiologies but may also have common pathways contributing to ED. Such pathways may be potential treatment targets".

- Treatment possibility of hypercholesterolaemia associated with hypertriglyceridaemis with Acipimox:

Paragh et al(PubMed Abstract 9406614, also cited as Acta Biol. Hung., 48/3,359-67(1997)) state that:" Patients with NIDDM had increase in HDL-C, while patients with primary hyperlipoproteinaemia did not change significantly. The low density lipoprotein(LDL) level did not change significantly in either groups of patients. ....Uric

acid levels decreased significantly in NIDDM group. Serum glucose level did not change in the non-diabetic patients, while it decreased significantly in the NIDDM group".

12. Specification in pages 26-27(see Example 3) describes tests/ assays performed on a mce by oral administration of the instant compound(s) and a comparative compound as disclosed in WO 9728813 (= 2-(1,2,3,4,-tetrahydroxybutyl)-5-(2',3',4'-trihydroxybutyl)-pyrazine). This compound is the free alcohol base used for the instant compounds which are esters. The comparative results will only demonstrate the improvement(s) obtained over the existing compounds which are used as starting material(s) for the instantly claimed compounds. Thus the reference is not art recongnized pharmaceutical.

13. Such results and assays will only serve for the preliminary screening of many compounds, and not for treating the diseases or complications as claimed herein.

14. The facts as provided above do support the need for additional quantity of experimentation, which would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the method of not only treatment, but also prevention of various disorders/conditions related to diabetes.

15. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of instant compounds to control or prevent disorders related to inflammation

16. When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ

609. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

Conclusion

Allowable Subject Matter

17. Claims 1-13 related to compounds and composition would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

18. The following is a statement of reasons for the indication of allowable subject matter: The closest prior art ref. Tsuchida et al teaches 1,2,3-butanetriol, 4-[6-(hydroxymethyl)-5-(1,2,3-trihydroxypropyl) pyrazinyl]-. Tsuchida differs from the instant compounds by having second chain/bridge as propyl instead of instantly claimed butane bridge, and also0 the end hydroxyl groups are not esterified by 5 or 6-membered saturated cycloalkyl carboxylic acid groups.

19. The other reference art of record Ratsimanga et al (WO 97 28813) teaches 2,5-di-tetrahydoxybutyl pyrazine(see page 8), and 2-tetrahydroxybutyl-6-trihydoxybutyl pyrazine(see page 10). The ref. '813 differs from the instant compounds by not having the end –OH groups esterified by 5 or 6-membered saturated alkyl ring(s).

20. Neither Tsichida et al not ref.' 813 indicate or suggest to arrive at the instant invention.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker B. Patel, D.Sc.Tech. whose telephone number is 703 308 4709. The examiner can normally be reached on 6:30 to 5:00 pm (Monday-Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund J. Shah can be reached on 703 308 4716 or Sr. Examiner Mr. Richard Raymond at (703) 308 4523.

The fax phone numbers for the organization where this application or proceeding is assigned are 703 308 4556 for regular communications and 703 308 4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1235.

Sudhaker B. Patel, D.Sc.Tech.
November 18, 2003.

MUKUND SHAH
SUPERVISORY PATENT EXAMINER
ART UNIT 1624